

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES

PLEASE LOGON:

***** HHHHHHHH SSSSSSSS? ### Status: Signing onto Dialog *****

ENTER PASSWORD:

***** HHHHHHHH SSSSSSSS? *****

Status: Login successfulWelcome to DIALOG

Dialog level 05.05.00D

Last logoff: 08jun05 14:19:29

Logon file405 13jul05 10:41:15

*** ANNOUNCEMENT ***

--UPDATED: Important Notice to Freelance Authors--

See HELP FREELANCE for more information

NEW FILES RELEASED

***Aluminium Industry Abstracts (File 33)

***Ceramic Abstracts/World Ceramic Abstracts (File 335)

***CSA Life Sciences Abstracts (File 24)

***Corrosion Abstracts (File 46)

***Materials Business File (File 269)

***Engineered Materials Abstracts (File 293)

***CSA Aerospace & High Technology Database (File 108)

***CSA Technology Research Database (File 23)

***METADEX(r) (File 32)

***FDAnews (File 182)

***German Patents Fulltext (File 324)

RESUMED UPDATING

***Canadian Business and Current Affairs (262)

***CorpTech (559)

Chemical Structure Searching now available in Proux Science Drugs
of the Future (F453), IMS R&D Focus (F445), Beilstein Facts (F390),
and Derwent Chemistry Resource (F355).

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<

>>> of new databases, price changes, etc. <<<

KWIC is set to 50.

HIGHLIGHT set on as '*'

PICKS is set ON as an alias for

5,159,143,358,340,344,348,447,73,155,349,266,10,34,434,42,43,50,65,71,91,94,14

4,198,304,370,467,444,357,156,157.

* * *

SYSTEM:HOME

Cost is in DialUnits

Menu System II: D2 version 1.7.9 term=ASCII

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. Data Star(R)

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/H = Help

/L = Logoff

/NOMENU = Command Mode

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?

Terminal set to DLINK

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
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/H = Help

/L = Logoff

/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

? B picks

```
>>>          43 does not exist
>>>1 of the specified files is not available
      13jul05 10:41:24 User243038 Session D128.1
          $0.00    0.214 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.03 TELNET
$0.03 Estimated cost this search
$0.03 Estimated total session cost  0.214 DialUnits
```

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2005/Jul W1

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File 159:Cancerlit 1975-2002/Oct

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***File 159: Cancerlit is no longer updating.**

Please see HELP NEWS159.

File 143:Biol. & Agric. Index 1983-2005/Jun

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File 358:Current BioTech Abs 1983-2005/Jun

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File 340:CLAIMS(R)/US Patent 1950-05/Jul 07
 (c) 2005 IFI/CLAIMS(R)
 File 344:Chinese Patents Abs Aug 1985-2005/May
 (c) 2005 European Patent Office
 File 348:EUROPEAN PATENTS 1978-2005/Jun W04
 (c) 2005 European Patent Office
 File 447:IMS Patent Focus 2005/Jun
 (c) 2005 IMS Health & Affiliates
 File 73:EMBASE 1974-2005/Jul 12
 (c) 2005 Elsevier Science B.V.
 File 155:MEDLINE(R) 1951-2005/Jul W2
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 File 266:FEDRIP 2005/Jun
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 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
 (c) 1998 Inst for Sci Info
 File 42:Pharmaceuticl News Idx 1974-2005/Jun W4
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 File 71:ELSEVIER BIOBASE 1994-2005/Jul W1
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 2001 (c) Action Potential
 File 94:JICST-EPlus 1985-2005/May W4
 (c)2005 Japan Science and Tech Corp(JST)
 File 144:Pascal 1973-2005/Jul W1
 (c) 2005 INIST/CNRS
 File 198:Health Devices Alerts(R) 1977-2005/Jul W1
 (c) 2005 ECRI-nonprft agncy
 File 304:The Merck Index Online(SM) 200(c) 2005 Merck & Co. Inc.
 5/S1
***File 304: File is now current to the 13th edition of The Merck Index**
 File 370:Science 1996-1999/Jul W3
 (c) 1999 AAAS
***File 370: This file is closed (no updates). Use File 47 for more current information.**
 File 467:ExtraMED(tm) 2000/Dec
 (c) 2001 Informania Ltd.
***File 467: F467 no longer updates; see Help News467.** 7.
 File 444:New England Journal of Med. 1985-2005/Jun W4
 (c) 2005 Mass. Med. Soc.
 File 357:Derwent Biotech Res. 1982-2005/Jul W2
 (c) 2005 Thomson Derwent & ISI
 File 156:ToxFile 1965-2005/Jul W2
 (c) format only 2005 The Dialog Corporation
***File 156: ToxFile has been reloaded with the 2005 MeSH.**
 Please see HELP NEWS 156 for details.
 File 157:BIOSIS Toxicology (c) 2004 BIOSIS

Set Items Description

? s level of transcription
S1 1 LEVEL OF TRANSCRIPTION
? t s1

1/2/1 (Item 1 from file: 5)
DIALOG(R) File 5: Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.

0014120784 BIOSIS NO.: 200300079503

Mitogen activated protein kinase phosphatases-1 and -2 are differentially regulated at the level of transcription in cultured rat cardiac ventricular myocytes.

AUTHOR: Fuller Stephen J (Reprint); Finn Stephen G (Reprint)
AUTHOR ADDRESS: NHLI London, London, UK**UK
JOURNAL: Circulation 106 (19 Supplement): pII-205 November 5, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Abstracts from Scientific Sessions Chicago, IL, USA
November 17-20, 2002; 20021117
SPONSOR: American Heart Association
ISSN: 0009-7322 (ISSN print)
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 306298-47-5: mitogen-activated protein kinase phosphatase
1; 306748-07-2: mitogen-activated protein kinase phosphatase 2;
16561-29-8: 12-O-tetradecanoyl phorbol 13-acetate; 50-76-0: actinomycin
D

DESCRIPTORS:

MAJOR CONCEPTS: Cardiovascular System--Transport and Circulation; Cell
Biology; Enzymology--Biochemistry and Molecular Biophysics; Molecular
Genetics--Biochemistry and Molecular Biophysics
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata,
Animalia
ORGANISMS: rat (Muridae)--neonate
ORGANISMS: PARTS ETC: ventricular myocyte--circulatory system, *level of
transcription*
COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates
; Nonhuman Mammals; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: mitogen-activated protein kinase phosphatase
1; mitogen-activated protein kinase phosphatase 2; 12-O-tetradecanoyl
phorbol 13-acetate; actinomycin D
GENE NAME: rat c-Jun gene (Muridae); rat c-Fos gene (Muridae)
METHODS & EQUIPMENT: Western blot--genetic techniques, laboratory
techniques

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings
02502 Cytology - General
02506 Cytology - Animal
03502 Genetics - General
03506 Genetics - Animal
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
10802 Enzymes - General and comparative studies: coenzymes
14504 Cardiovascular system - Physiology and biochemistry

BIOSYSTEMATIC CODES:

86375 Muridae

? t TGF beta transcription

>>>'TGF' not recognized as set or accession number

? t transforming growth factor beta transcription
>>>'TRANSFORMING' not recognized as set or accession number
? s CtBP

S2 1292 CTBP
? s s2 and Smad
1292 S2
12514 SMAD
S3 53 S2 AND SMAD

? rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.
>>>Duplicate detection is not supported for File 198.
>>>Duplicate detection is not supported for File 304.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records (50)
...completed examining records
S4 19 RD (unique items)

? t s4/all
>>>'ALL' not allowed as format type
? t s4/t/5
>>>'T' not a valid format name
? t s4/3

4/3/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
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0014936627 BIOSIS NO.: 200400307384

**Proteins associated with type II bone morphogenetic protein receptor
(BMPR-II) and identified by two-dimensional gel electrophoresis and mass
spectrometry**

AUTHOR: Hassel Sylke; Eichner Annegret; Yakymovych Mariya; Hellman Ulf;
Knaus Petra; Souchelnytskyi Serhiy (Reprint)
AUTHOR ADDRESS: BMC, Ludwig Inst Canc Res, Box 595, Husargatan 3, SE-75124,
Uppsala, Sweden**Sweden

AUTHOR E-MAIL ADDRESS: serhiy.souchelnytskyi@licr.uu.se

JOURNAL: Proteomics 4 (5): p1346-1358 May 2004 2004

MEDIUM: print

ISSN: 1615-9853 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

? t s4/all/5

>>>'ALL' not allowed as format type

? t s4/ab/5

>>>No matching display code(s) found in file(s): 65, 198, 304, 447

4/AB/5 (Item 5 from file: 5)

DIALOG(R)File 5:(c) 2005 BIOSIS. All rts. reserv.

ABSTRACT: Although Evi-1 is thought to promote growth or block
differentiation in some cell types, its biological functions have not
been elucidated. To explore the mechanisms underlying Evi-1-induced
oncogenesis, we investigated whether Evi-1 affects the signaling of
transforming growth factor beta (TGF-beta), which inhibits proliferation

of a wide range of cell types and is one of the most studied growth regulatory factors. We demonstrated that Evi-1 represses TGF-beta signaling and antagonizes its growth-inhibitory effects. Two separate regions of Evi-1 are responsible for this repression, one of which is the first zinc-finger domain. Through this domain, Evi-1 physically interacts with Smad3, an intracellular mediator of TGF-beta signaling, thereby suppressing the transcriptional activity of Smad3. These results define a novel function of Evi-1 as a repressor of signaling components of TGF-beta. We also demonstrated that Evi-1 represses *Smad*-induced transcriptional activation by recruiting *CtBP* as a corepressor. Evi-1 associates with CtBP1 through one of the *CtBP*-binding consensus motifs within the region from amino acid 544 to 607, and this association is required for the efficient inhibition of TGF-beta signaling. A specific histone deacetylase (HDAC) inhibitor, trichostatin A (TSA), alleviates Evi-1-mediated repression of TGF-beta signaling, suggesting that HDAC is involved in transcriptional repression by Evi-1. This identifies a novel function of Evi-1 as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms involved in Evi-1-induced leukemogenesis. These results indicate that specific HDAC inhibitors may be useful in the treatment of Evi-1-induced neoplastic tumors, including myeloid leukemias.

? t s4/all/all

>>>'ALL' not allowed as format type

? t s4/3,ab

>>>No matching display code(s) found in file(s): 65, 198, 304, 447

4/3,AB/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2005 BIOSIS. All rts. reserv.

0014936627 BIOSIS NO.: 200400307384

Proteins associated with type II bone morphogenetic protein receptor (BMPR-II) and identified by two-dimensional gel electrophoresis and mass spectrometry

AUTHOR: Hassel Sylke; Eichner Annegret; Yakymovych Mariya; Hellman Ulf; Knaus Petra; Souchelnytskyi Serhiy (Reprint)

AUTHOR ADDRESS: BMC, Ludwig Inst Canc Res, Box 595, Husargatan 3, SE-75124, Uppsala, Sweden**Sweden

AUTHOR E-MAIL ADDRESS: serhiy.souchelnytskyi@licr.uu.se

JOURNAL: Proteomics 4 (5): p1346-1358 May 2004 2004

MEDIUM: print

ISSN: 1615-9853 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Bone morphogenetic proteins (BMP) are polypeptide growth factors that regulate cell differentiation and proliferation. BMPs bind to type I and type II serine/threonine kinase receptors to initiate intracellular signalling. BMPR-II is the type II receptor, its mutations lead to hereditary pulmonary hypertension, and knockout of Bmpr-II results in early embryonic lethality. To identify novel interacting proteins and explore signalling pathways that can be initiated by BMPR-II, we performed glutathione-S-transferase (GST) pull-down assays with BMPR-II protein constructs fused to GST and extracts of mouse myoblast C2C12 cells. We generated three constructs which contain different parts of the cytoplasmic region of BMPR-II: full-length cytoplasmic part of BMPR-II, only the kinase domain, or only the C-terminal tail of BMPR-II. Proteins which formed complexes with these BMPR-II constructs were analyzed by

two-dimensional gel electrophoresis (2-D GE), and specifically interacting proteins were identified by matrix-assisted laser desorption/ionization-time of flight-mass spectrometry (MALDI-TOF-MS). We identified 33 interacting proteins; 11 proteins interacted with the C-terminal tail of BMPR-II, 4 with full-length BMPR-II, and 18 with a short form of the receptor with a deleted tail. Fourteen proteins have assigned functions in various signalling processes, suggesting links of BMP signalling to regulation of MAP kinase pathway, apoptosis, transcription, PKCbeta, and PKA. Five of the identified proteins are components of the cytoskeleton, and four are enzymes involved in metabolism, e.g., processing of estrogens or lipids. We confirmed interaction of PKCbeta and *CtBP* with BMPR-II using immunodetection. We showed that the C-terminal tail of BMPR-II provides binding sites for a number of regulatory proteins that may initiate *Smad*-independent signalling.

? t s4/abs

>>>"ABS" is not a valid format name in file(s): 5, 10, 34, 42, 50, 65, 71, 73, 91, 94, 143-144, 155-157, 159, 198, 266, 304, 340, 344, 348-349, 357-358, 370, 434, 444, 447, 467

? t s4/3,ab/all

>>>No matching display code(s) found in file(s): 65, 198, 304, 447

4/3,AB/1 (Item 1 from file: 5)

DIALOG(R)File 5:BIOSIS Previews(R)

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0014936627 BIOSIS NO.: 200400307384

Proteins associated with type II bone morphogenetic protein receptor (BMPR-II) and identified by two-dimensional gel electrophoresis and mass spectrometry

AUTHOR: Hassel Sylke; Eichner Annegret; Yakymovych Mariya; Hellman Ulf; Knaus Petra; Souchelnytskyi Serhiy (Reprint)

AUTHOR ADDRESS: BMC, Ludwig Inst Canc Res, Box 595,Husargatan 3, SE-75124, Uppsala, Sweden**Sweden

AUTHOR E-MAIL ADDRESS: serhiy.souchelnytskyi@licr.uu.se

JOURNAL: Proteomics 4 (5): p1346-1358 May 2004 2004

MEDIUM: print

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C-terminal tail of BMPR-II, 4 with full-length BMPR-II, and 18 with a short form of the receptor with a deleted tail. Fourteen proteins have assigned functions in various signalling processes, suggesting links of BMP signalling to regulation of MAP kinase pathway, apoptosis, transcription, PKCbeta, and PKA. Five of the identified proteins are components of the cytoskeleton, and four are enzymes involved in metabolism, e.g., processing of estrogens or lipids. We confirmed interaction of PKCbeta and *CtBP* with BMPR-II using immunodetection. We showed that the C-terminal tail of BMPR-II provides binding sites for a number of regulatory proteins that may initiate *Smad*-independent signalling.

4/3,AB/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0014652262 BIOSIS NO.: 200400023019

Smad6 recruits transcription corepressor *CtBP* to repress bone morphogenetic protein-induced transcription.

AUTHOR: Lin Xia (Reprint); Liang Yao-Yun; Sun Baohua; Liang Min; Shi Yujiang; Brunicardi F Charles; Shi Yang; Feng Xin-Hua

AUTHOR ADDRESS: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, Room 131D, Houston, TX, 77030, USA**USA

AUTHOR E-MAIL ADDRESS: xialin@bcm.tmc.edu; xfeng@bcm.tmc.edu

JOURNAL: Molecular and Cellular Biology 23 (24): p9081-9093 December 2003

MEDIUM: print

ISSN: 0270-7306 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Smad6 and Smad7 are inhibitory Smads induced by transforming growth factor beta-*Smad* signal transduction pathways in a negative-feedback mechanism. Previously it has been thought that inhibitory Smads bind to the type I receptor and block the phosphorylation of receptor-activated Smads, thereby inhibiting the initiation of *Smad* signaling. Conversely, few studies have suggested the possible nuclear functions of inhibitory Smads. Here, we present compelling evidence demonstrating that Smad6 repressed bone morphogenetic protein-induced Id1 transcription through recruiting transcriptional corepressor C-terminal binding protein (*CtBP*). A consensus *CtBP*-binding motif, PLDLs, was identified in the linker region of Smad6. Our findings show that mutation in the motif abolished the Smad6 binding to *CtBP* and subsequently its repressor activity of transcription. We conclude that the nuclear functions and physical interaction of Smad6 and *CtBP* provide a novel mechanism for the transcriptional regulation by inhibitory Smads.

4/3,AB/3 (Item 3 from file: 5)

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0014447731 BIOSIS NO.: 200300406450

Interaction between *Smad*-interacting protein-1 and the corepressor C-terminal binding protein is dispensable for transcriptional repression of E-cadherin.

AUTHOR: van Grunsven Leo A; Michiels Christine; Van de Putte Tom; Nelles Luc; Wuytens Gunther; Verschueren Kristin (Reprint); Huylebroeck Danny
AUTHOR ADDRESS: Dept. of Developmental Biology, Laboratory of Molecular Biology (Celgen), Flanders Interuniversity Institute for Biotechnology (VIB), University of Leuven, Herestraat 49, VIB7, Campus Gasthuisberg (Bldg. O and N), B-3000, Leuven, Belgium**Belgium
AUTHOR E-MAIL ADDRESS: Kristin.Verschueren@med.kuleuven.ac.be
JOURNAL: Journal of Biological Chemistry 278 (28): p26135-26145 July 11, 2003 2003
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: deltaEF1 and SIP1 (or Zfhx1a and Zfhx1b, respectively) are the only known members of the vertebrate Zfh1 family of homeodomain/zinc finger-containing proteins. Similar to other transcription factors, both *Smad*-interacting protein-1 (SIP1) and deltaEF1 are capable of repressing E-cadherin transcription through binding to the E2 boxes located in its promoter. In the case of deltaEF1, this repression has been proposed to occur via interaction with the corepressor C-terminal binding protein (*CtBP*). In this study, we show by coimmunoprecipitation that SIP1 and *CtBP* interact in vivo and that an isolated *CtBP*-binding SIP1 fragment depends on *CtBP* for transcriptional repression. However, and most importantly, full-length SIP1 and deltaEF1 proteins do not depend on their interaction with *CtBP* to repress transcription from the E-cadherin promoter. Furthermore, in E-cadherin-positive kidney epithelial cells, the conditional synthesis of mutant SIP1 that cannot bind to *CtBP* abrogates endogenous E-cadherin expression in a similar way as wild-type SIP1. Our results indicate that full-length SIP1 can repress E-cadherin in a *CtBP*-independent manner.

4/3,AB/4 (Item 4 from file: 5)
DIALOG(R) File 5:Biosis Previews(R)
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0014354932 BIOSIS NO.: 200300312421

Regulation of *Smad* signaling through a differential recruitment of coactivators and corepressors by ZEB proteins.

AUTHOR: Postigo Antonio A (Reprint); Depp Jennifer L; Taylor Jennifer J; Kroll Kristen L
AUTHOR ADDRESS: Division of Molecular Oncology, Department of Internal Medicine, Washington University School of Medicine, Saint Louis, MO, 63110, USA**USA
AUTHOR E-MAIL ADDRESS: apostigo@im.wustl.edu
JOURNAL: EMBO (European Molecular Biology Organization) Journal 22 (10): p 2453-2462 May 15, 2003 2003
MEDIUM: print
ISSN: 0261-4189 (ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Balancing signals derived from the TGFbeta family is crucial for regulating cell proliferation and differentiation, and in establishing the embryonic axis during development. TGFbeta/BMP signaling leads to the activation and nuclear translocation of *Smad* proteins, which activate

transcription of specific target genes by recruiting P/CAF and p300. The two members of the ZEB family of zinc finger factors (ZEB-1/deltaE1 and ZEB-2/SIPI) regulate TGFbeta/BMP signaling in opposite ways: ZEB-1/deltaE1 synergizes with *Smad*-mediated transcriptional activation, while ZEB-2/SIPI represses it. Here we report that these antagonistic effects by the ZEB proteins arise from the differential recruitment of transcriptional coactivators (p300 and P/CAF) and corepressors (*CtBP*) to the Smads. Thus, while ZEB-1/deltaE1 binds to p300 and promotes the formation of a p300-*Smad* transcriptional complex, ZEB-2/SIPI acts as a repressor by recruiting *CtBP*. This model of regulation by ZEB proteins also functions in vivo, where they have opposing effects on the regulation of TGFbeta family-dependent genes during Xenopus development.

4/3,AB/5 (Item 5 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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0013352192 BIOSIS NO.: 200100524031

Oncogenic mechanisms of Evi-1 protein

AUTHOR: Hirai Hisamaru (Reprint); Izutsu Koji; Kurokawa Mineo; Mitani Kinuko

AUTHOR ADDRESS: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo, 113-8655, Japan**Japan

JOURNAL: Cancer Chemotherapy and Pharmacology 48 (Supplement 1): pS35-S40 August, 2001 2001

MEDIUM: print

ISSN: 0344-5704

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Although Evi-1 is thought to promote growth or block differentiation in some cell types, its biological functions have not been elucidated. To explore the mechanisms underlying Evi-1-induced oncogenesis, we investigated whether Evi-1 affects the signaling of transforming growth factor beta (TGF-beta), which inhibits proliferation of a wide range of cell types and is one of the most studied growth regulatory factors. We demonstrated that Evi-1 represses TGF-beta signaling and antagonizes its growth-inhibitory effects. Two separate regions of Evi-1 are responsible for this repression, one of which is the first zinc-finger domain. Through this domain, Evi-1 physically interacts with Smad3, an intracellular mediator of TGF-beta signaling, thereby suppressing the transcriptional activity of Smad3. These results define a novel function of Evi-1 as a repressor of signaling components of TGF-beta. We also demonstrated that Evi-1 represses *Smad*-induced transcriptional activation by recruiting *CtBP* as a corepressor. Evi-1 associates with CtBP1 through one of the *CtBP*-binding consensus motifs within the region from amino acid 544 to 607, and this association is required for the efficient inhibition of TGF-beta signaling. A specific histone deacetylase (HDAC) inhibitor, trichostatin A (TSA), alleviates Evi-1-mediated repression of TGF-beta signaling, suggesting that HDAC is involved in transcriptional repression by Evi-1. This identifies a novel function of Evi-1 as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms involved in Evi-1-induced leukemogenesis. These results indicate that specific HDAC inhibitors may be useful in the treatment of Evi-1-induced neoplastic

tumors, including myeloid leukemias.

4/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013129631 BIOSIS NO.: 200100301470

The corepressor *CTBP* is involved in Evi-1 mediated repression of TGF-beta signaling

AUTHOR: Izutsu Koji (Reprint); Kurokawa Mineo (Reprint); Imai Yoichi (Reprint); Mitani Kinuko (Reprint); Hirai Hisamaru (Reprint)
AUTHOR ADDRESS: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan**Japan
JOURNAL: Blood 96 (11 Part 1): p90a November 16, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Evi-1 is a zinc finger nuclear protein whose inappropriate expression leads to leukemic transformation of hematopoietic cells in mice and humans. Evi-1 is shown to be highly expressed in human myeloid leukemias and myelodysplastic syndromes by chromosomal rearrangements involving 3q26. It is also aberrantly expressed as a fusion transcript with AML1 (AML1/Evi-1), which leads to blastic transformation in patients with chronic myelogenous leukemia. We previously showed that Evi-1 and AML1/Evi-1 block the antiproliferative effect of TGF-beta. They represses TGF-beta signaling by direct interaction with Smad3 through their first zinc finger motif. Here, we demonstrate that Evi-1 represses *Smad*-induced transcription by recruiting *CtBP* as a corepressor. *CtBP* was originally identified as a protein which interacts with C-terminal region of adenoviral oncoprotein E1A. *CtBP* is ubiquitously expressed including hematopoietic cells, and has been shown to act as a corepressor of certain transcriptional repressors, such as BKLf, FOG, and TCF. We show that Evi-1 directly associates with CtBP1 through one of the consensus binding motifs, and this association is required for efficient inhibition of TGF-beta signaling. A specific inhibitor for histone deacetylase (HDAC) alleviates Evi-1-mediated repression of TGF-beta signaling, suggesting that HDAC is involved in the transcriptional repression by Evi-1. This identifies a novel function of Evi-1 as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms for Evi-1-induced leukemogenesis.

4/3,AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013072727 BIOSIS NO.: 200100244566

The corepressor *CtBP* interacts with Evi-1 to repress transforming growth factor beta signaling

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JOURNAL: Blood 97 (9): p2815-2822 May 1, 2001 2001
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Evi-1 is a zinc finger nuclear protein whose inappropriate expression leads to leukemic transformation of hematopoietic cells in mice and humans. This was previously shown to block the antiproliferative effect of transforming growth factor beta (TGF-beta). Evi-1 represses TGF-beta signaling by direct interaction with Smad3 through its first zinc finger motif. Here, it is demonstrated that Evi-1 represses *Smad*-induced transcription by recruiting C-terminal binding protein (*CtBP*) as a corepressor. Evi-1 associates with CtBP1 through one of the consensus binding motifs, and this association is required for efficient inhibition of TGF-beta signaling. A specific inhibitor for histone deacetylase (HDAC) alleviates Evi-1-mediated repression of TGF-beta signaling, suggesting that HDAC is involved in the transcriptional repression by Evi-1. This identifies a novel function of Evi-1 as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms for Evi-1-induced leukemogenesis.

4/3,AB/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0012889338 BIOSIS NO.: 200100061177

The interaction of the carboxyl terminus-binding protein with the *Smad* corepressor TGIF is disrupted by a holoprosencephaly mutation in TGIF

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JOURNAL: Journal of Biological Chemistry 275 (50): p39762-39766 December 15, 2000 2000

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ISSN: 0021-9258

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RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The homeodomain protein TGIF represses transcription in part by recruiting histone deacetylases. TGIF binds directly to DNA to repress transcription or interacts with TGF-beta-activated Smads, thereby repressing genes normally activated by TGF-beta. Loss of function mutations in TGIF result in holoprosencephaly (HPE) in humans. One HPE mutation in TGIF results in a single amino acid substitution in a conserved PLDLS motif within the amino-terminal repression domain. We demonstrate that TGIF interacts with the corepressor carboxyl terminus-binding protein (*CtBP*) via this motif. *CtBP*, which was first identified by its ability to bind the adenovirus E1A protein, interacts both with gene-specific transcriptional repressors and with a subset of polycomb proteins. Efficient repression of TGF-beta-activated gene responses by TGIF is dependent on interaction with *CtBP*, and we show that TGIF is able to recruit *CtBP* to a TGF-beta-activated *Smad* complex. Disruption of the PLDLS motif in TGIF abolishes the interaction

of *CtBP* with TGIF and compromises the ability of TGIF to repress transcription. Thus, at least one HPE mutation in TGIF appears to prevent *CtBP*-dependent transcriptional repression by TGIF, suggesting an important developmental role for the recruitment of *CtBP* by TGIF.

4/3,AB/9 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
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Dialog Acc No: 10193957 IFI Acc No: 2002-0137662
IFI Publication Control No: 2002-0137662 IFI Chemical Acc No: 2002-0035621
Document Type: C

**COMPOSITIONS AND METHODS FOR NEGATIVE REGULATION OF TGF-BETA PATHWAYS;
IDENTIFYING COMPOUNDS THAT DIRECTLY INTERACT WITH *SMAD* PROTEINS, OR WITH
SMAD CO-REPRESSORS, TO PREVENT PROTEIN-PROTEIN OR PROTEIN-DNA
INTERACTIONS REQUIRED FOR TRANSCRIPTIONAL REPRESSION IN RESPONSE TO TGF,
ACTIVIN**

Inventors: Laughon Allen S (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Kind,Date), Applic (No,Date):
US 20020137662 A1 20020926 US 2001810385 20010316
Priority Applic(No,Date): US 2001810385 20010316

Abstract: Methods for screening for compounds that are negative regulators of TGF- beta -regulated gene expression in mammalian cells are provided, including compositions identified therefrom.

4/3,AB/10 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE
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12346566 EMBASE No: 2003457732

TGIF2 Interacts with Histone Deacetylase I and Represses Transcription

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Journal of Biological Chemistry (J. BIOL. CHEM.) (United States) 24

AUG 2001, 276/34 (32109-32114)

CODEN: JBCHA ISSN: 0021-9258

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 49

TG-interacting factor (TGIF) is a transcriptional repressor, which represses transcription by binding directly to DNA or interacts with transforming growth factor alpha (TGFbeta)-activated Smads, thereby repressing TGFbeta-responsive gene expression. Mutation of TGIF in humans causes holoprosencephaly, a severe genetic disorder affecting craniofacial development. Searching human expressed sequence tag data bases revealed the presence of clones encoding a TGIF-related protein (TGIF2), which contains two regions of high sequence identity with TGIF. Here we show that, like TGIF, TGIF2 recruits histone deacetylase, but in contrast to TGIF, is unable to interact with the corepressor *CtBP*. TGIF2 and TGIF have very similar DNA-binding homeodomains, and TGIF2 represses transcription when

bound to DNA via a TGIF binding site. TGIF2 interacts with TGFbeta-activated Smads and represses TGFbeta-responsive transcription. TGIF2 appears to be a context-independent transcriptional repressor, which can perform similar functions to TGIF and may play a role in processes, which, when disrupted by mutations in TGIF, cause holoprosencephaly.

4/3,AB/11 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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18120834 PMID: 15849193

Repression of bone morphogenetic protein and activin-inducible transcription by Evi-1.

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Journal of biological chemistry (United States) Jun 24 2005, 280 (25) p24227-37, ISSN 0021-9258 Journal Code: 2985121R

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Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Smads, key effectors of transforming growth factor (TGF)-beta, activin, and bone morphogenetic protein (BMP) signaling, regulate gene expression and interact with coactivators and corepressors that modulate *Smad* activity. The corepressor Evi-1 exerts its oncogenic effects by repressing TGF-beta/Smad3-mediated transcription, thereby blocking TGF-beta-induced growth arrest. Because Evi-1 interacts with the highly conserved MH2 domain of Smad3, we investigated the physical and functional interaction of Evi-1 with Smad1 and Smad2, downstream targets of BMP and activin signaling, respectively. Evi-1 interacted with and repressed the receptor-activated transcription through Smad1 and Smad2, similarly to Smad3. In addition, Evi-1 repressed BMP/Smad1- and activin/Smad2-mediated induction of endogenous Xenopus gene expression, suggesting a role of repression of BMP and activin signals by Evi-1 in vertebrate embryogenesis. Evi-1 also repressed the induction of endogenous Smad7 expression by TGF-beta family ligands. In the course of these studies, we observed Evi-1 repression of *Smad* transactivation even when *Smad* binding to DNA was kept constant. We therefore explored the mechanism of Evi-1 repression of TGF-beta family-inducible transcription. Evi-1 repression did not result from displacement of *Smad* binding to DNA or to CREB-binding protein but from the recruitment of Evi-1 by Smad3 and CREB-binding protein to DNA. Following TGF-beta stimulation, Evi-1 and the associated corepressor *CtBP* were recruited to the endogenous Smad7 promoter. Evi-1 recruitment to the promoter decreased TGF-beta-induced histone acetylation, coincident with its repression of Smad7 gene expression. In this way, Evi-1 acts as a general *Smad* corepressor to inhibit TGF-beta-, activin-, and BMP-inducible transcription.

4/3,AB/12 (Item 1 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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01116723

**BINARY PREDICTION TREE MODELING WITH MANY PREDICTORS AND ITS USES IN
CLINICAL AND GENOMIC APPLICATIONS**

**MODELISATION D'UN ARBRE PREVISIONNEL BINAIRE A PLUSIEURS PREDICTEURS, ET
SON UTILISATION DANS DES APPLICATIONS CLINIQUES ET GENOMIQUES**

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200438376 A2-A3 20040506 (WO 0438376)

Application: WO 2003US33946 20031024 (PCT/WO US03033946)

Priority Application: US 2002420729 20021024; US 2002421062 20021025; US
2002421102 20021025; US 2002424715 20021108; US 2002424718 20021108; US
2002424701 20021108; US 2002425256 20021112; US 2003448462 20030221; US
2003448461 20030221; US 2003457877 20030327; US 2003458373 20030331

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC
SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 300141

English Abstract

Provided is a statistical analysis method that is a predictive
statistical tree model. This model first screens genes to reduce noise,
applies k-means correlation-based clustering, and then uses
singular-value decompositions to extract the single dominant factor
(principal component) from each cluster. This generates a statistically
significant number of cluster-derived singular factors, that we refer to
as metagenes, which characterize multiple patterns of expression of the
genes across samples. The strategy aims to extract multiple such patterns
while reducing dimension and smoothing out gene[specific noise through
the aggregation within clusters. Formal predictive analysis then uses
these metagenes in a Bayesian classification tree analysis. This
generates multiple recursive partitions of the sample into subgroups
("leaves" of the tree), and associates Bayesian predictive probabilities
of outcomes with each subgroup. Overall predictions for an individual

sample are then generated by averaging predictions, with appropriate weights, across many such tree models. The model includes the use of iterative out-of-sample cross-validation predictions to perform refitting of the model, and mirrors the real-world prognostic context where prediction of new cases as they arise is the major goal.

French Abstract

L'invention porte sur une analyse statistique sous forme de modele statistique previsionnel d'arborescence resolvant plusieurs problemes observes dans des modeles statistiques anterieurs et des analyses de regression, tout en offrant une precision et des capacites previsionnelles ameliorees. Bien que le modele de l'invention serve principalement a pronostiquer les maladie d'individus, il peut egalement etre utilise dans une variete d'applications dont: la prevision des stades de maladies ou de la susceptibilite d'y arriver, tout autre etat biologique d'interet, et d'autres etats non biologiques d'interet. Le modele de l'invention crible d'abord les genes pour reduire le bruit, applique k moyens d'agglutination a base de correlation a un grand nombre d'utilisations, puis procede a une decomposition en valeurs singulieres pour extraire le facteur dominant unique (composant principal) de chacun des amas. Cela cree un nombre statistiquement significatif de facteurs singuliers, dits metagenes caracterisant de multiples schema d'expression des genes dans les echantillons. La strategie vise a extraire nombre de ces schemas tout en reduisant les dimensions et lissant le bruit specifique des genes en les agregeant en amas. L'analyse predictive formelle utilise alors ces metagenes pour une analyse par arbre Bayesien de classification. Cela cree de multiples separations recursives de l'echantillon en sous-groupes (les feuilles de l'arbre de classification) et les probabilites previsionnelles associees Bayesiennes des resultats pour chaque sous-groupe. Les previsions generales relatives a un echantillon individuel sont alors etablies par moyennage avec des poids appropries en utilisant plusieurs de ces modeles d'arborescence. Le modele de l'invention utilise des pronostics iteratifs hors echantillonnage et des pronostics a validation croisee, laissant chaque echantillon un par un hors de l'ensemble de donnees, rajustant le modele a partir des echantillons restants et l'utilisant pour pronostiquer les cas a ecarter. Cela verifie ainsi rigoureusement les valeurs previsionnelles d'un modele et reflete le contexte des pronostics en temps reel alors que les previsions sur les nouveaux cas se presentant est l'objectif majeur.

4/3,AB/13 (Item 2 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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01094160

**EXPANSION OF CELLS USING THROMBOPOIETIN AND ANTI-TRANSFORMING GROWTH
FACTOR-BETA**

**DEVELOPPEMENT DE CELLULES UTILISANT LA THROMBOPOIETINE ET UN
ANTI-FACTEUR-BETA DE CROISSANCE TRANSFORMANT**

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Patent and Priority Information (Country, Number, Date):

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Priority Application: US 2002213957 20020807

Parent Application/Grant:

Related by Continuation to: US 2002213957 20020807 (CON)

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(Protection type is "patent" unless otherwise stated - for applications
prior to 2004)

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD
SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 16936

English Abstract

The invention features a method for the expansion of hematopoietic stem cells using a combination of a thrombopoietin agonist and a transforming growth factor- beta blocking agent in the absence of stem cell factor. The invention also features a hematopoietic stem cell composition that has been expanded using a combination of a thrombopoietin agonist and a transforming growth factor-beta blocking agent in the absence of stem cell factor, as well as methods of using an expanded hematopoietic stem cell composition to restore or supplement an immune system and/or blood forming system compromised by, for example, radiation or chemotherapy.

French Abstract

L'invention concerne un procede de developpement de cellules souches hematopoietiques utilisant une combinaison d'un agoniste de thrombopoietine et d'un agent bloquant le facteur beta de croissance transformant en l'absence de facteur de cellules souches. L'invention concerne egalement une composition de cellules souches hematopoietiques ayant ete developpees au moyen d'une combinaison d'un agoniste de thrombopoietine et d'un agent bloquant le facteur beta de facteur transformant en l'absence de facteur de cellules souches ainsi que des procedes d'utilisation d'une composition de cellules souches hematopoietiques developpees pour retablir ou completer un systeme immun et/ou un systeme hematopoietique defaillant, par exemple, par rayonnement ou chimiotherapie.

4/3,AB/14 (Item 3 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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01044797

RNA INTERFERENCE MEDIATED INHIBITION OF GENE EXPRESSION USING SHORT
INTERFERING NUCLEIC ACID (SINA)

INTERFERENCE ARN PERMETTANT D'INHIBER L'EXPRESSION D'UN GENE A L'AIDE D'UN
ACIDE NUCLEIQUE INTERFERANT COURT (SINA)

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Patent and Priority Information (Country, Number, Date):

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Priority Application: US 2002358580 20020220; US 2002363124 20020311; US
2002386782 20020606; US 2002406784 20020829; US 2002408378 20020905; US
2002409293 20020909; US 2003440129 20030115

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Related by Continuation to: US 2002358580 20020220 (CON); US 2002363124
20020311 (CON); US 2002386782 20020606 (CON); US 2002406784 20020829
(CON); US 2002408378 20020905 (CON); US 2002409293 20020909 (CON); US
2003440129 20030115 (CON)

Designated States:

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG
SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT SE SI
SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 262755

English Abstract

The present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid molecules, such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) molecules capable of mediating RNA interference (RNAi) against target nucleic acid sequences. The small nucleic acid molecules are useful in the treatment of any disease or

condition that responds to modulation of gene expression or activity in a cell, tissue, or organism.

French Abstract

L'invention concerne des methodes et des reactifs utilises pour moduler une expression genique dans une variete d'applications, notamment dans des applications therapeutiques, diagnostiques, de validation de cible et de decouverte genomique. L'invention concerne, plus specifiquement, de petites molecules d'acide nucleique, tel qu'un acide nucleique d'interference court (INA), un ANR d'interference court (siRNA), un ARN double brins (dsRNA), un micro-ARN (miRNA) et des molecules d'ARN court en epingle a cheveux (shRNA) capables d'induire une mediation d'interference ARN (RNAi) par rapport a des sequences cibles d'acide nucleique. On utilise ces petites molecules d'acide nucleiques pour traiter une maladie ou un etat quelconque repondant a la modulation de l'expression d'un gene ou d'une activite dans une cellule, un tissu, ou un organisme.

4/3,AB/15 (Item 4 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00942700

COMPOSITIONS AND METHODS FOR NEGATIVE REGULATION OF TGF-BETA PATHWAYS COMPOSITIONS ET PROCEDES POUR LA REGULATION NEGATIVE DES VOIES DE FACTEUR DE CROISSANCE TRANSFORMANT BETA

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Patent and Priority Information (Country, Number, Date):

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Priority Application: US 2001810385 20010316

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 4842

English Abstract

Methods for screening for compounds that are negative regulators of TGF-beta-regulated gene expression in mammalian cells are provided, including compositions identified therefrom.

French Abstract

La presente invention concerne des procedes de criblage de composes qui sont des regulateurs negatifs de l'expression genetique regulee de TGF-beta dans des cellules mammaliennes, ainsi que des compositions qui sont identifiees a partir de ceux-ci. FIG. 1 : A beta-GALACTOSIDASE B 5 NANOGRAMMES DE MAD/20 NANOGRAMMES DE MEDEA C 0 NANOGRAMMES DE MEDEA, 0 NANOGRAMMES DE MAD D NANOGRAMMES DE LA PROTEINE dCtB

4/3,AB/16 (Item 5 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00739915

GENE EXPRESSION IN BLADDER TUMORS

EXPRESSION GENIQUE DANS LES TUMEURS DE LA VESSIE

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200052204 A2-A3 20000908 (WO 0052204)

Application: WO 2000IB367 20000222 (PCT/WO IB0000367)

Priority Application: US 99121124 19990222

Parent Application/Grant:

Related by Continuation to: US 99121124 19990222 (CON)

Designated States:

(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

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Fulltext Word Count: 161096

English Abstract

Methods for analyzing tumor cells, particularly bladder tumor cells employ gene expression analysis of samples. Gene expression patterns are formed and compared to reference patterns. Alternatively gene expression patterns are manipulated to exclude genes which are expressed in contaminating cell populations. Another alternative employs subtraction of the expression of genes which are expressed in contaminating cell types. These methods provide improved accuracy as well as alternative basis for analysis from diagnostic and prognostic tools currently available.

French Abstract

L'invention concerne des procedes d'analyse des cellules cancéreuses, particulierement des cellules cancéreuses de la vessie recourant a l'analyse genique d'échantillons. Les modeles d'expression genique sont formes et compares a des modeles de reference. Selon une variante, les

modeles d'expression genique sont manipules pour exclure les genes qui sont exprimes dans des populations de cellules contaminantes. Selon une autre variante, on utilise la soustraction de l'expression des genes qui sont exprimes dans des types de cellules contaminantes. Ces procedes assurent une plus grande precision et servent de base pour l'analyse a partir d'outils de diagnostic et de pronostic disponibles sur le marche.

4/3,AB/17 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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11659340 Genuine Article#: 680BU Number of References: 66

Title: Opposing functions of ZEB proteins in the regulation of the TGF beta/BMP signaling pathway (ABSTRACT AVAILABLE)

Author(s): Postigo AA (REPRINT)

Corporate Source: Washington Univ,Sch Med, Dept Internal Med, Div Mol Oncol,St Louis//MO/63110 (REPRINT); Washington Univ,Sch Med, Dept Internal Med, Div Mol Oncol,St Louis//MO/63110

Journal: EMBO JOURNAL, 2003, V22, N10 (MAY 15), P2443-2452

ISSN: 0261-4189 Publication date: 20030515

Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Binding of TGFbeta/BMP factors to their receptors leads to translocation of *Smad* proteins to the nucleus where they activate transcription of target genes. The two-handed zinc finger proteins encoded by Zfhx1a and Zfhx1b, ZEB-1/deltaEF1 and ZEB-2/SIP1, respectively, regulate gene expression and differentiation programs in a number of tissues. Here I demonstrate that ZEB proteins are also crucial regulators of TGFbeta/BMP signaling with opposing effects on this pathway. Both ZEB proteins bind to Smads, but while ZEB-1/deltaEF1 synergizes with *Smad* proteins to activate transcription, promote osteoblastic differentiation and induce cell growth arrest, the highly related ZEB-2/SIP1 protein has the opposite effect. Finally, the ability of TGFbeta to mediate transcription of TGFbeta-dependent genes and induce growth arrest depends on the presence of endogenous ZEB-1/deltaEF1 protein.

4/3,AB/18 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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10819811 Genuine Article#: 571XC Number of References: 52

Title: Overlapping and unique roles for C-terminal binding protein 1 (CtBP1) and CtBP2 during mouse development. (ABSTRACT AVAILABLE)

Author(s): Hildebrand JD (REPRINT) ; Soriano P

Corporate Source: Univ Pittsburgh,Dept Biol Sci,5th & Ruskin Ave/Pittsburgh//PA/15260 (REPRINT); Univ Pittsburgh,Dept Biol Sci,Pittsburgh//PA/15260; Fred Hutchinson Canc Res Ctr,Program Dev Biol,Seattle//WA/98108; Fred Hutchinson Canc Res Ctr,Div Basic Sci,Seattle//WA/98108

Journal: MOLECULAR AND CELLULAR BIOLOGY, 2002, V22, N15 (AUG), P5296-5307

ISSN: 0270-7306 Publication date: 20020800

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA

Language: English Document Type: ARTICLE

Abstract: The C-terminal binding protein (*CtBP*) family of proteins has been linked to multiple biological processes through their association

with numerous transcription factors. We generated mice harboring mutations in both Ctbpl and Ctbp2 to address the in vivo function of CtBPs during vertebrate development. Ctbpl mutant mice are small but viable and fertile, whereas Ctbp2-null mice show defects in axial patterning and die by E10.5 due to aberrant extraembryonic development. Mice harboring various combinations of Ctbpl and Ctbp2 mutant alleles exhibit dosage-sensitive defects in a wide range of developmental processes. The strong genetic interaction, as well as transcription assays with *CtBP*-deficient cells, indicates that CtBPs have overlapping roles in regulating gene expression. We suggest that the observed phenotypes reflect the large number of transcription factors whose activities are compromised in the absence of *CtBP*.

4/3,AB/19 (Item 1 from file: 357)

DIALOG(R) File 357:Derwent Biotech Res.

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0323067 DBR Accession No.: 2003-24207 PATENT

Identifying compounds that interact with *Smad* protein (co-repressor),
useful for treating diseases involving negative regulation of
transforming growth factor-beta e.g. cancer and autoimmune disease -
involving vector-mediated gene transfer and expression in host cell for
use in drug screening

AUTHOR: LAUGHON A S

PATENT ASSIGNEE: LAUGHON A S 2002

PATENT NUMBER: US 20020137662 PATENT DATE: 20020926 WPI ACCESSION NO.:
2003-657220 (200362)

PRIORITY APPLIC. NO.: US 810385 APPLIC. DATE: 20010316

NATIONAL APPLIC. NO.: US 810385 APPLIC. DATE: 20010316

LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Identifying compounds that directly interact with a *Smad* protein or a *Smad* protein co-repressor to prevent protein-protein or protein-DNA interactions required for repression of transcription induced by transforming growth factor (TGF)-beta, activin or bone morphogenetic protein (BMP) signaling in cells, is new. DETAILED DESCRIPTION - Identifying compounds that directly interact with a *Smad* protein or a *Smad* protein co-repressor to prevent protein-protein or protein-DNA interactions required for repression of transcription induced by transforming growth factor (TGF)-beta, activin or bone morphogenetic protein (BMP) signaling in cells comprising: (a) determining a first level of transcription detected in cells in the presence of a *Smad* protein and a *CtBP* (undefined) protein before addition of a test compound; (b) contacting the cells with the test compound; and (c) determining a second level of transcription detected in cells in the presence of a *Smad* protein and a *CtBP* protein after addition of the test compound, where a decrease in the level of repression of transcription induced by the presence of the *Smad* protein and the *CtBP* protein is indicative of the ability of the test compound to interfere with transcriptional repression and to prevent repression of transcription that is produced by a TGF-beta, activin, or BMP signal in cells. INDEPENDENT CLAIMS are also included for the following: (1) a composition identified by the method; and (2) identifying a candidate gene that is directly and negatively regulated by TGF-beta signaling pathways through a *CtBP* protein comprising: (a) determining a first level of TGF-beta-regulated target gene expression in the presence of *CtBP* ; (b) determining a second level of TGF-beta-regulated target gene expression in the absence of the *CtBP* protein; and (c) comparing

the first level of expression with the second level of expression, where dependence of TGF-beta-regulated gene expression on the presence of the *CtBP* protein is indicative of the ability of the candidate gene to be directly and negatively regulated by *CtBP* working in conjunction with the *Smad* protein. BIOTECHNOLOGY - Preferred Method: Transcription levels both before and after addition of the test compound are detected in cells in the presence of a *Smad* protein, a *CtBP* protein, and a co-repressor protein such as Evi-1, TGIF (undefined), SIP1 (undefined), and Schnurri. The *Smad* protein is Drosophila Mad or Medea. The *CtBP* protein is dCtBP (preferred), CtBP2 or any homolog of *CtBP*. ACTIVITY - Cytostatic; Immunosuppressive. MECHANISM OF ACTION - *CtBP* inhibitor; *Smad* inhibitor; Negative regulator of TGF-beta. No biological data given. USE - The compounds or genes identified through such assays would be useful in the development of drugs and therapeutics for treatment of cancer, autoimmune diseases, and other hereditary diseases that involve negative regulation by TGF-beta pathways. (7 pages)

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Set	Items	Description
S1	1	LEVEL OF TRANSCRIPTION
S2	1292	CTBP
S3	53	S2 AND SMAD
S4	19	RD (unique items)
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